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Incidence and Clinical Impact of Stent Fracture After PROMUS Element Platinum Chromium Everolimus-Eluting Stent Implantation

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ABSTRACT

OBJECTIVES This study sought to assess the incidence and clinical impact of stent fracture (SF) after the PROMUS Element platinum-chromium everolimus-eluting stent (PtCr-EES).

BACKGROUND SF remains an unresolved, clinically relevant issue, even in the newer-generation drug-eluting stent era.

METHODS From March 2012 to August 2013, 816 patients with 1,094 lesions were treated only with PtCr-EES and 700 patients (85.7%) with 898 lesions undergoing follow-up angiography within 9 months after the index procedure were analyzed. SF was defined as complete or partial separation of the stent, as assessed by plain fluoroscopy, intravascular ultrasound, or optical coherence tomography during the follow-up. We assessed the rate of SF and the cumulative incidence of clinically driven target lesion revascularization and definite stent thrombosis within 9 months after the index procedure.

RESULTS SF was observed in 16 of 898 lesions (1.7%) and 16 of 700 patients (2.2%). Lesions with in-stent restenosis at baseline (odds ratio [OR]: 14.2, 95% confidence intervals [CI]: 5.09 to 39.7; $p < 0.001$) or hinge motion (OR: 4.31, 95% CI: 1.12 to 16.5; $p = 0.03$), and total stent length (per 10-mm increase; OR: 1.32, 95% CI: 1.12 to 1.57; $p = 0.001$) were predictors of SF. Cumulative incidence of clinically driven target lesion revascularization within 9-months was numerically higher in the SF group than that in the non-SF group (18.7% vs. 2.3%). Cumulative incidence of definite stent thrombosis within 9 months after the index procedure was similar between the SF and non-SF groups (0.0% vs. 0.23%).

CONCLUSIONS SF after PtCr-EES occurs in 1.7% of lesions and appears to be associated with clinically driven target lesion revascularization. (J Am Coll Cardiol Intv 2015;8:1180–8) © 2015 by the American College of Cardiology Foundation.

Drug-eluting stents (DES) have dramatically reduced the rates of in-stent restenosis (ISR) and subsequent target lesion revascularization (TLR) compared with bare-metal stents (BMS) (1). However, widespread use of first-generation DES has drawn attention to several unresolved, clinically relevant issues. Particular concerns have been raised about the risks of DES, especially stent thrombosis (ST) (2,3). Stent fracture (SF) after DES implantation has recently become an important concern because of its potential association with ISR, TLR, and ST (4). The incidence of SF in the clinical setting has been reported to be 0.84% to 8.4% in first-generation DES (5,6). In the newer-generation

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DES, we previously reported that SF after cobalt chromium everolimus-eluting stent (CoCr-EES) implantation occurs in 2.9% of lesions and is associated with a higher rate of major adverse cardiac events, driven by higher rates of TLR and ST (7). More recently, we also reported SF after the Nobori biolimus-eluting stent (BES) (Terumo, Tokyo, Japan) implantation occurs in 4.1% of lesions, and the incidence of TLR is higher in the SF lesion compared with the non-SF lesion (8). Therefore, SF is still an unresolved, clinically relevant issue even in the newer-generation DES era.

The platinum-chromium everolimus-eluting stent (PtCr-EES) is a newer-generation DES that uses the same drug and polymer as CoCr-EES but combines them with a novel metal alloy and stent design intended to improve deliverability, conformability, radiopacity, radial strength, and fracture resistance (9). The PLATINUM trial (A Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of Up to Two de Novo Coronary Artery Lesions) showed that the clinical outcome after PtCr-EES implantation was noninferior to that after CoCr-EES for up to 3 years (10,11). Furthermore, the DUTCH PEERS (Durable Polymer-Based Stent Challenge of Promus Element Versus Resolute Integrity in an All Comers Population) trial demonstrated that PtCr-EES and CoCr zotarolimus-eluting stents were similarly efficacious and safe, and provided excellent clinical outcomes in an all-comer population (12). However, the incidence and clinical impact of SF after PtCr-EES implantation remain unclear. The aim of the present study was to assess the incidence and clinical impact of SF after PtCr-EES implantation.

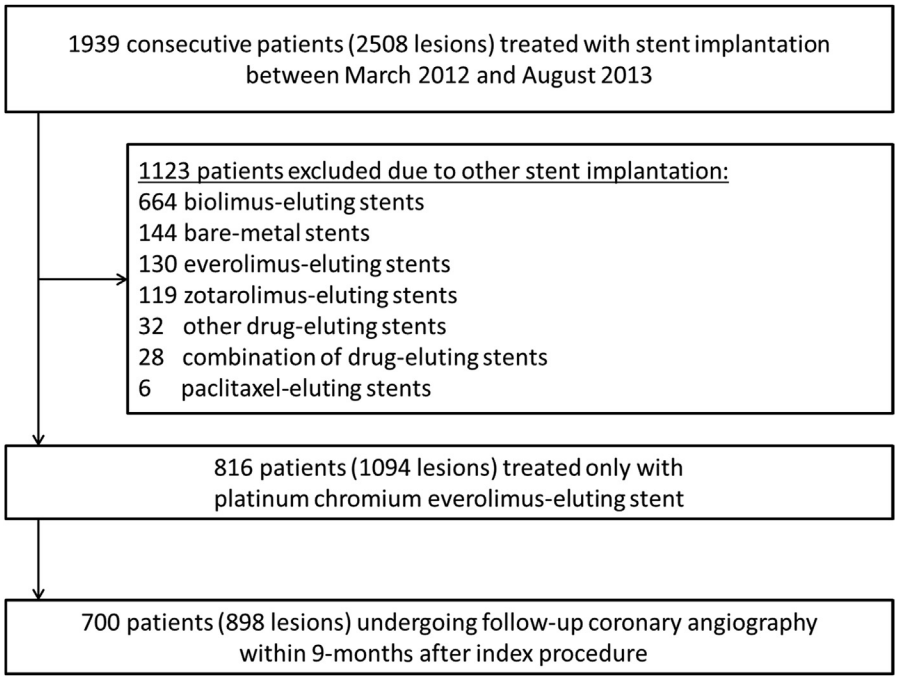
METHODS

PATIENT POPULATION AND PROCEDURAL PROTOCOL. From March 2012 to August 2013, 1,939 consecutive patients with 2,508 lesions underwent successful stent implantation, and 816 patients with 1,094 lesions were treated only with PtCr-EES (PROMUS Element, Boston Scientific, Natick, Massachusetts) at Kokura Memorial Hospital. Of these, 700 patients (85.7%) with 898 lesions who underwent follow-up angiography 6 to 9 months after the initial procedure, irrespective of clinical symptoms, or before 6 months for recurrent symptoms, were enrolled in this study (Figure 1). All interventions were performed using standard

ABBREVIATIONS AND ACRONYMS

BES = biolimus-eluting stent
BMS = bare-metal stent(s)
CoCr-EES = cobalt chromium everolimus-eluting stent
DES = drug-eluting stent(s)
ISR = in-stent restenosis
IVUS = intravascular ultrasound
LSD = longitudinal stent deformation
OCT = optical coherence tomography
PtCr-EES = platinum-chromium everolimus-eluting stent
SES = sirolimus-eluting stent(s)
SF = stent fracture
ST = stent thrombosis
TLR = target lesion revascularization

FIGURE 1 Study Flow Chart



techniques. Pre-dilation, post-dilation, and use of intravascular ultrasound (IVUS) and optical coherence tomography (OCT) were left to the operator's discretion. After the procedure, all patients were advised to continue on aspirin (81 to 162 mg daily) for life unless there were contraindications. Either ticlopidine (200 mg daily) or clopidogrel (75 mg daily) was also prescribed for at least 1 year after stent implantation. All the study patients gave written informed consent for the procedure and the follow-up protocol, which was approved by the Institutional Review Board of Kokura Memorial Hospital.

QUANTITATIVE ANGIOGRAPHIC ANALYSIS. Coronary angiography was performed after the intracoronary administration of 0.2 mg of nitroglycerin. Quantitative coronary angiographic analysis was performed before and after stenting and during follow-up angiography, using a guiding catheter to calibrate the magnification and a validated automated edge-detection algorithm (CASS 5.7, Pie Medical Imaging, Eindhoven, the Netherlands). The analyses were performed independently by 2 experienced observers of the Angiographic Core Laboratory, Kokura Memorial Hospital, blinded to the clinical information. The target lesion for measurement of the minimal luminal diameter included 5-mm margins proximal and distal to the stent as well as the stent itself. ISR was defined as a percent diameter stenosis of >50% within the stent at the time of follow-up. In-segment restenosis was defined as a percent diameter stenosis of >50% either within the stented segment or within the 5 mm proximal or distal to the stent segment. The angiographic ISR patterns were classified as focal or diffuse according to Mehran's classification (13). A hinge-motion lesion was defined as having ≥16° difference in angle between diastole and systole before the procedure (14).

TABLE 1 Baseline Patient Characteristics

	Overall (N = 700)	SF (n = 16)	Non-SF (n = 684)	p Value
Age, yrs	69.7 ± 9.7	69.1 ± 6.7	69.6 ± 9.7	0.84
Male	511 (73.0)	11 (68.7)	500 (73.1)	0.77
Hypertension	562 (80.0)	13 (81.2)	549 (80.2)	>0.99
Diabetes	320 (45.5)	7 (43.7)	313 (45.7)	>0.99
Dyslipidemia	580 (82.6)	13 (81.2)	567 (82.8)	0.74
Hemodialysis	71 (10.1)	4 (25.0)	67 (9.8)	0.07
Current smoking	120 (17.1)	4 (25.0)	116 (16.9)	0.49
Multivessel disease	202 (28.9)	5 (31.2)	197 (28.8)	0.78
No. of diseased vessels				0.64
1	499 (71.1)	11 (68.7)	488 (71.3)	
2	175 (25.0)	5 (31.2)	170 (24.9)	
3	26 (3.7)	0 (0.0)	26 (3.8)	
Previous MI	140 (19.9)	4 (25.0)	136 (19.8)	0.53
Previous PCI	314 (44.7)	8 (50.0)	306 (44.7)	0.80
Previous CABG	36 (5.1)	1 (6.2)	35 (5.1)	0.57
Previous CI	53 (7.6)	1 (6.2)	52 (7.6)	>0.99
Clinical status				0.58
Stable angina	611 (87.3)	14 (87.5)	597 (87.3)	
Unstable angina	20 (2.8)	0 (0.0)	20 (2.9)	
AMI	69 (9.8)	2 (12.5)	67 (9.8)	
LVEF, %	59.9 (50.6–65.9)	53.0 (41.3–62.7)	60.0 (51.0–66.1)	0.014
Medical treatment				
Aspirin	700 (100.0)	16 (100.0)	684 (100.0)	–
Thienopyridine	699 (99.8)	16 (100.0)	683 (99.8)	>0.99
Statins	541 (77.0)	11 (68.7)	530 (77.4)	0.37
ACE-I	132 (18.8)	6 (37.5)	126 (18.4)	0.09
ARB	311 (44.3)	7 (43.7)	304 (44.4)	>0.99
β-Blockers	293 (41.9)	9 (56.2)	284 (41.5)	0.30
OHA	240 (34.1)	4 (25.0)	236 (34.5)	0.59
Insulin	63 (8.9)	1 (6.2)	62 (9.0)	>0.99

Values are mean ± SD, n (%), or median (interquartile range [IQR]).

ACE-I = angiotensin-converting enzyme inhibitor; AMI = acute myocardial infarction; ARB = angiotensin receptor blocker; CABG = coronary artery bypass graft; CI = cerebral infarction; LVEF = left ventricular ejection fraction; MI = myocardial infarction; OHA = oral hypoglycemia agent; PCI = percutaneous coronary intervention; SF = stent fracture.

STUDY ENDPOINT AND DEFINITIONS. The study primary endpoint was the incidence of SF within 9 months after PtCr-EES implantation. The secondary endpoint was the cumulative incidence of clinically driven TLR and definite ST within 9 months after the index procedure. A clinically driven TLR was defined as a >70% diameter stenosis on follow-up angiography in the presence of signs or symptoms of myocardial ischemia. The timing and diagnostic certainty of ST were assessed according to the Academic Research Consortium definition (15).

SF was defined as complete or partial separation of stent segments observed by plain fluoroscopy without contrast injection, IVUS, or OCT at follow-up angiography (8). The angiographic diagnosis of SF required an independent review and the agreement of 2 independent cardiologists (T.H. and S.E.). Angiographic SF was classified as follows: type 1 (partial separation), type 2 (complete separation without displacement), or type 3a and 3b (complete separation with displacement) (9). Diagnosis of SF by IVUS or OCT required careful review of the IVUS or OCT images and the agreement of 2 independent cardiologists (T.D. and M.H.). SF observed by IVUS and OCT was classified as complete (complete separation of the stent into ≥2 pieces separated by image slices with no visible struts) or partial (the absence of struts over one-half or more of the stent circumference).

STATISTICAL ANALYSIS. Data are presented as values and percentages, mean ± SD, or median (interquartile range [IQR]). Categorical variables were

compared between groups with the chi-square test or Fisher exact test, as appropriate. Continuous variables were compared between groups using the Student unpaired *t* test or the Mann-Whitney *U* test, on the basis of the distribution. For the lesion-based analysis of the risk factors for SF, we used unadjusted and multivariable-adjusted logistic regression models with random intercepts that accounted for the clustered nature of lesion characteristics within patients. The following 6 variables with $p < 0.05$ in the univariate analysis were tested for their multivariable predictive value: ISR at baseline, hinge motion, right coronary artery, total stent length (per 10-mm increase), tortuosity, and stent overlap. The final model was constructed using the 4 variables: ISR at baseline, hinge motion, right coronary artery, and total stent length (per 10-mm increase) selected by forward stepwise method in standard logistic regression program, with both entry and exit criteria set at the $p = 0.05$ level. Cumulative incidence of clinically driven TLR, and ST within 9 months after the index procedure, between lesions with SF and those without SF was estimated by the Kaplan-Meier method. Because of the small number of events in the SF and non-SF groups, statistical comparisons were not conducted for the cumulative event rates. All statistical analyses were performed by a physician (S.K.) and a statistician (T.S.) using JMP version 10.0.2 and SAS version 9.4 (SAS Institute, Cary, North Carolina). Random-intercept logistic models were fitted through the pseudo-likelihood method on the basis of outcome linearization in the SAS GLIMMIX procedure and other analyses were carried out in JMP software. A 2-sided p value of <0.05 was considered statistically significant.

RESULTS

Of 816 patients, 700 patients (85.7%) with 898 lesions who underwent follow-up angiography 6 to 9 months after the initial procedure, irrespective of clinical symptoms, or before 6 months for recurrent symptoms, were enrolled in this study (**Figure 1**). Coronary angiography was performed 190 days (IQR: 183 to 234 days) after the index procedure. Baseline characteristics of the 700 patients with follow-up angiography included in this study were not significantly different from those of the 116 patients without angiography except for age, male sex, dyslipidemia, left ventricular ejection fraction, and statin use (Online Table 1). At follow-up, SF after PtCr-EES implantation was recognized in 16 of 898 lesions (1.7%) and in 16 of 700 patients (2.2%). In 15 of the 16 lesions (93.7%), SF was found at a single point, whereas SF occurred in 2 or more points per lesion in 1 lesion (6.3%). As a result, a total of 18 fractures in 16 lesions was observed.

TABLE 2 Baseline Lesion Characteristics

	Overall (N = 898)	SF (n = 16)	Non-SF (n = 882)	p Value
Location of target lesion				0.025
RCA	326 (36.1)	13 (81.2)	313 (35.2)	
LAD	370 (40.9)	2 (12.5)	368 (41.4)	
LCX	195 (21.5)	1 (6.3)	194 (21.8)	
LMT	7 (0.7)	0 (0.0)	7 (0.7)	
SVG	3 (0.3)	0 (0.0)	3 (0.3)	
LITA	1 (0.1)	0 (0.0)	1 (0.1)	
GEA	1 (0.1)	0 (0.0)	1 (0.1)	
Lesion type				0.07
A	44 (5.3)	0 (0.0)	44 (5.4)	
B1	247 (29.9)	4 (28.5)	243 (30.0)	
B2	187 (22.6)	0 (0.0)	187 (23.0)	
C	346 (41.9)	10 (71.4)	336 (41.4)	
In-stent restenosis	82 (9.0)	7 (43.7)	74 (8.3)	<0.001
Calcification	77 (8.5)	2 (12.5)	75 (8.5)	0.64
Tortuosity	427 (47.5)	12 (75.0)	415 (47.0)	0.04
Hinge motion	274 (30.5)	11 (68.7)	263 (29.8)	0.001
Bifurcation	236 (26.2)	2 (12.5)	234 (26.5)	0.26
Ostial location	17 (1.8)	1 (6.2)	16 (1.8)	0.26
Chronic total occlusion	72 (8.0)	2 (12.5)	70 (7.9)	0.37
Stent diameter, mm	2.8 ± 0.4	2.9 ± 0.4	2.8 ± 0.4	0.37
Total stent length, mm	24.0 (20.0–38.0)	48.0 (21.0–62.0)	24.0 (20.0–38.0)	0.018
No. of stents per lesion				0.002
1	683 (76.1)	7 (43.8)	676 (76.6)	
2	172 (19.1)	6 (37.5)	166 (18.8)	
≥3	43 (4.8)	3 (18.7)	40 (4.5)	
Maximal pressure, atm	15.1 ± 4.2	16.3 ± 3.0	15.1 ± 4.2	0.10
Post dilation	443 (49.3)	10 (62.5)	433 (49.0)	0.32
Stent overlap	204 (22.7)	9 (56.2)	195 (22.1)	0.003
Use of IVUS or OCT	881 (98.1)	15 (93.7)	866 (98.1)	0.26
QCA results				
Lesion length, mm	26.0 ± 12.9	37.0 ± 17.2	25.8 ± 12.8	0.004
RVD at baseline, mm	2.58 ± 0.40	2.61 ± 0.52	2.58 ± 0.39	0.78
Pre-MLD, mm	0.63 ± 0.37	0.60 ± 0.48	0.63 ± 0.37	0.94
Pre-%DS, %	71.8 ± 15.0	75.5 ± 19.5	71.7 ± 14.9	0.63
Post-MLD, mm	2.17 ± 0.36	2.12 ± 0.47	2.17 ± 0.36	0.61
Post-%DS, %	15.8 ± 6.7	18.8 ± 7.2	15.8 ± 6.6	0.07
In-stent restenosis				
Focal	82 (9.1)	7 (43.7)	75 (8.5)	<0.001
Diffuse	14 (1.6)	2 (12.5)	12 (1.3)	<0.001
Overall	96 (10.7)	9 (56.2)	87 (9.8)	<0.001
In-segment restenosis	104 (11.6)	9 (56.2)	95 (10.8)	<0.001

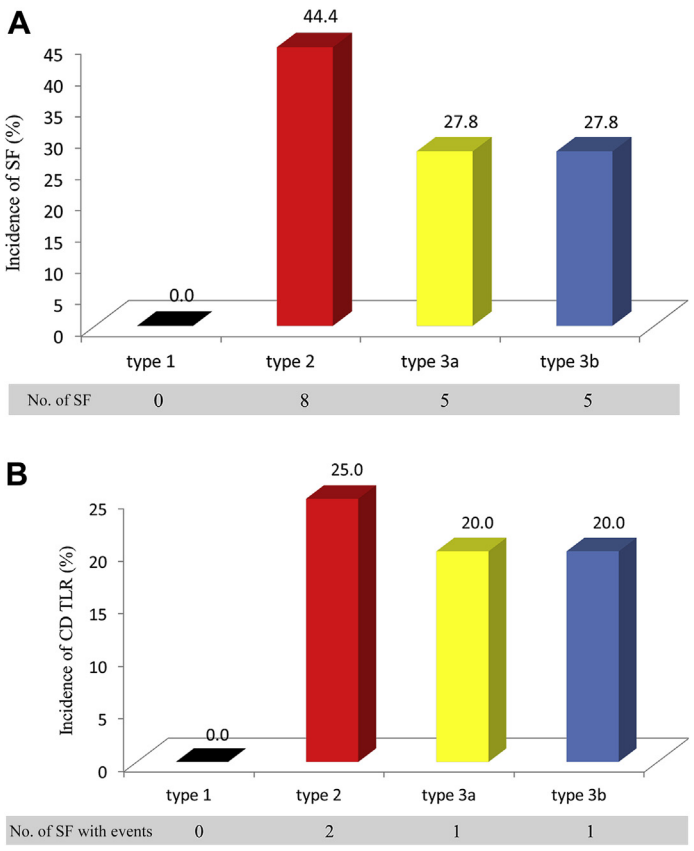
Values are n (%), mean ± SD, or median (IQR).

DS = diameter stenosis; GEA = gastroepiploic artery; IVUS = intravascular ultrasound; LAD = left anterior coronary artery; LCX = left circumflex coronary artery; LITA = left internal thoracic artery; LMT = left main trunk; MLD = minimal lumen diameter; OCT = optical coherence tomography; QCA = quantitative coronary angiography; RCA = right coronary artery; RVD = reference vessel diameter; SVG = saphenous vein graft; other abbreviations as in Table 1.

CLINICAL CHARACTERISTICS. The baseline clinical characteristics of the SF and non-SF groups are shown in Table 1. There were no significant differences between the 2 groups except for left ventricular ejection fraction.

ANGIOGRAPHIC AND PROCEDURAL CHARACTERISTICS AND RESULTS. The angiographic and procedural characteristics and results of both groups are shown in Table 2. Compared with the non-SF group, the prevalence of the right coronary artery location, ISR at baseline, tortuosity, and hinge motion were significantly higher in the SF group. Index stent types that caused ISR at baseline included as follows: 33 BMS, 27 BES, 12 sirolimus-eluting stents (SES), 6 CoCr-EES, and 4 paclitaxel-eluting stents. Of these, 17 ISR (20.7%) were associated with SF (14 BES, 1 SES, 1 SES, and 1 CoCr-EES). Although stent size was similar between the 2 groups, significant differences were found in total stent length, number of stents per lesion, and the rate of lesions treated with ≥2 stents.

FIGURE 2 Angiographic Classification of SF and Clinical Outcome



(A) Classification of angiographic SF. **(B)** Relationships between angiographic SF classification and target lesion revascularization (TLR). CD = clinically driven; SF = stent fracture.

Pre-procedure lesion length was significantly longer in the SF group than in the non-SF group ($p = 0.004$). Post-procedure percent diameter stenosis tended to be higher in the SF group than in the non-SF group ($p = 0.07$). In SF lesions with hinge motion, the point of fracture was well accorded with the point of hinge motion. At follow-up, ISR and in-segment restenosis occurred more frequently in the SF group than in the non-SF group ($p < 0.001$). In the SF group, 56.2% of SF sites were associated with ISR at follow-up. The angiographic patterns of ISR at follow-up were mostly focal (85.4%) in both groups. Among 7 ISR lesions at follow-up in the SF group, 3 (42.9%) were ISR at baseline related to SF after BES implantation. In the remaining 4 ISR lesions (57.1%), all SFs occurred in the portion of previously implanted stent edge, leading to the point of hinge motion. No coronary aneurysm formation was observed in the SF group.

CLASSIFICATION AND INDEPENDENT PREDICTORS OF STENT FRACTURE. All SFs were angiographically visible SFs, in which 8 (44.4%) were type 2, 5 (27.8%) were type 3a, and 5 (27.8%) were type 3b (Figure 2A). Figure 2B show the classification of angiographic SF and the relationship between angiographic SF classification and TLR. Figure 3 and Online Figure 1 show representative cases with type 2, 3a, and 3b SFs. In the present study, 5 (27.8%) SFs were detected by using IVUS or OCT and performing a careful review of the angiogram. All SFs detected by using IVUS or OCT were complete fractures. The SFs were located in the mid-portion (50%), overlap portion (22.2%), proximal portion (16.7%), and distal portion (11.1%).

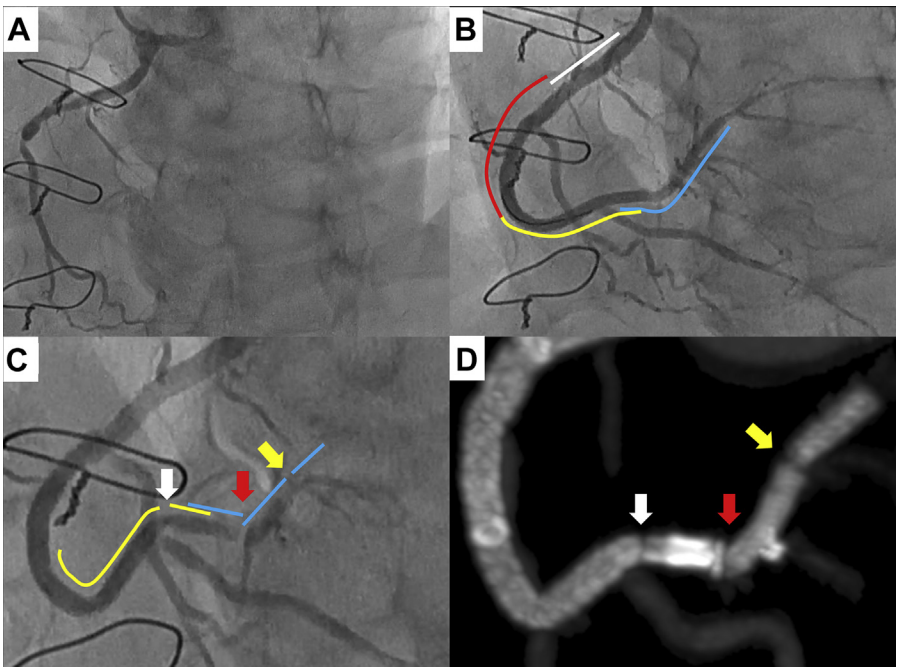
The predictors of SF after PtCr-EES implantation on multivariable logistic analysis are shown in Table 3. ISR at baseline (odds ratio [OR]: 14.2, 95% confidence interval [CI]: 5.09 to 39.7; $p < 0.001$), hinge motion (OR: 4.31, 95% CI: 1.12 to 16.5; $p = 0.03$), and total stent length (per 10-mm increase; OR: 1.32, 95% CI: 1.12 to 1.57; $p = 0.001$), were identified as predictors of SF after PtCr-EES implantation.

CLINICAL OUTCOMES. Clinically driven TLR was performed in 3 lesions with SF and 21 lesions without SF. Cumulative incidence of clinically driven TLR was numerically higher in the SF group than in the non-SF group (18.7% vs. 2.3%) (Figure 4). Although definite ST occurred in 2 lesions without SF (0.23%) at 5 and 32 days after PtCr-EES implantation, it did not occur in lesions with SF (Figure 5).

DISCUSSION

The main findings of the present study are: 1) the incidence of SF after PtCr-EES implantation was 1.7%

FIGURE 3 Representative Case of SF



(A) Coronary angiography shows a lesion with chronic total occlusion in the middle right coronary artery. **(B)** Final results after implantation of 4 platinum-chromium everolimus-eluting stents with overlap (3.5 × 20 mm **[white line]**, 3.5 × 38 mm **[red line]**, 2.5 × 28 mm **[yellow line]**, and 2.25 × 28 mm **[blue line]**). **(C)** At 6 months after implantation, angiography shows a total of 3 stent fractures (SFs) with 50% stenosis **(white arrow)**, 99% stenosis **(red arrow),** and total occlusion **(yellow arrow)** at the distal portion of the implanted stent. **(D)** Coronary computed tomography angiography shows type 2 SFs **(white and yellow arrows)** and type 3b SF **(red arrow)**.

of lesions; 2) SF appeared to be associated with higher rates of TLR; and 3) lesions with ISR at baseline, hinge motion, and total stent length were identified as predictors of SF.

The incidence of SF in the clinical setting has been reported to be 0.84% to 8.4% in first-generation DES (5,6). Of the newer-generation DES, we previously reported that SF after CoCr-EES and BES implantation was observed in 2.9% and 4.1% of lesions, respectively, and was associated with a higher rate of major cardiac events, mainly driven by higher TLR or ST (7,8). The PROMUS Element is a newer-generation DES with a novel metal alloy and stent design intended to improve deliverability and conformability, increase radial strength and radiopacity, and reduce recoil compared with previous DES. Bench testing indicates the PtCr-EES may be less likely than other DES to develop strut fracture over time (16). However, there are currently no data regarding the incidence and clinical impact of SF after PtCr-EES implantation. In the present study, despite a high prevalence of lesions with hinge motion or tortuosity, the incidence of SF after PtCr-EES implantation was 1.7% of lesions, which was lower than that after CoCr-EES and BES implantation (7,8). Therefore, PtCr-EES may be more resistant to fractures as compared with CoCr-EES and BES.

An optimal stent design incorporates a balance of desirable characteristics; however, an improvement in one feature may adversely affect other attributes of the stent platform. PtCr-EES is reportedly prone to longitudinal stent deformation (LSD) by adjunctive devices, instead of higher flexibility (17). Indeed, LSD occurred in 0.56% of lesions in the current study. The

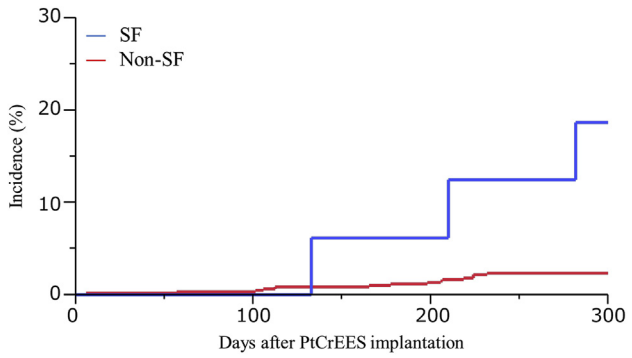
TABLE 3 Multivariable Logistic Regression Analysis of SF

	OR*	95% CI	p Value
In-stent restenosis at baseline	14.20	5.09-39.7	<0.001
Total stent length (per 10-mm increase)	1.32	1.12-1.57	0.001
Hinge motion	4.31	1.12-16.5	0.03
Right coronary artery	3.92	0.84-18.2	0.08

For all variables, $p < 0.05$ by unadjusted analysis with stent fracture (SF). *Random intercepts in the model accounted for within-patient clustering of lesion characteristics.

CI = confidence interval; OR = odds ratio.

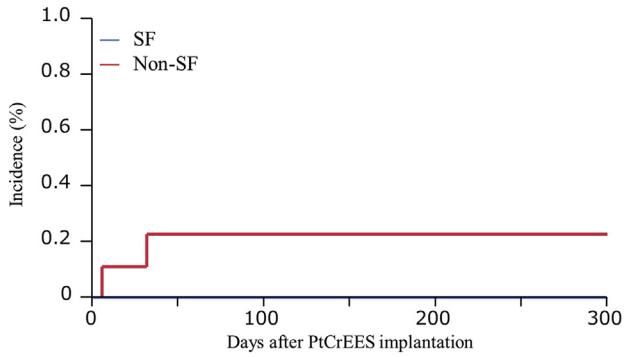
FIGURE 4 Cumulative Incidence Curves of Clinically Driven TLR Within 9 Months



Days	0	100	200	300
SF (+) N of lesions at risk	16	16	15	13
No. of lesions with events	0	0	1	3
Cumulative incidence	0%	0%	6.0%	18.7%
SF (-) N of lesions at risk	882	879	870	856
No. of lesions with events	0	3	12	21
Cumulative incidence	0%	0.3%	1.3%	2.3%

Blue line indicates SF patients; **red line**, non-SF patients. PtCrEES = platinum-chromium everolimus-eluting stent; other abbreviations as in Figure 2.

FIGURE 5 Cumulative Incidence Curves of Definite ST Within 9 Months



Days	0	100	200	300
SF (+) N of lesions at risk	16	16	16	16
No. of lesions with events	0	0	0	0
Cumulative incidence	0%	0%	0%	0%
SF (-) N of lesions at risk	882	880	880	875
No. of lesions with events	0	2	2	2
Cumulative incidence	0%	0.2%	0.2%	0.2%

Blue line indicates SF patients; **red line**, non-SF patients. ST = stent thrombosis; other abbreviations as in Figures 2 and 4.

contributors of SF are not only flexibility, but also longitudinal strength because repetitive cardiac contraction exposes the stent to compression, torsion, elongation, bending, and shear stress. These findings were supported by the presence of type 3b SF (8). Therefore, there is a little concern that type 3b SF might be likely to occur in PtCr-EES. In the present study, type 3b SF occurred in 27.8% of all SF lesions and was not more frequently observed in SF after PtCr-EES implantation. Moreover, it is intriguing that hinge motion was not the largest contributor to SF after PtCr-EES implantation, and tortuosity was not found to be a predictor, which were completely different results from CoCr-EES and BES (7,8). These findings suggest that flexibility plays the pivotal role in the incidence of SF rather than longitudinal strength, and some SFs are unavoidable even in PtCr-EES because the stent is made of metal. Nevertheless, if a de novo lesion was treated with a single stent, including the 38-mm PtCr-EES, the incidence of SF after PtCr-EES implantation was very rare (0.48%) in the present study. Therefore, PtCr-EES may reduce the incidence of SF to the utmost limit of a metallic DES.

SF has been associated with a higher potential risk of ISR, TLR, and ST in the first-generation DES (4). We previously reported that SF after CoCr-EES and BES implantation was associated with major adverse cardiac events within 9 months after the index procedure, primarily because of clinically driven TLR or ST (8,9). Similarly, the present study showed a higher incidence of clinically driven TLR after PtCr-EES implantation in the SF group compared with the non-SF group. Therefore, SF remains an issue even in PtCr-EES. On the other hand, ST did not occur in the SF group in the present study. Although the current study has a potential for underestimation because of a relatively small study population and the very low incidence of SF, the lack of ST might be due to differences in stent platform between PtCr-EES and other DES.

To date, there is no consensus regarding the optimal treatment for SF lesions. In the present study, a total of 16 SF lesions after implantation with other DES were treated with subsequent PtCr-EES implantation. Recurrent SF occurred in 3 (18.7%) of those SF lesions and was associated with a high rate of TLR (66.7%). Although it remains unclear which DES is suitable for the treatment of SF lesions, it should be recognized that some SF become refractory to PCI once it occurs. Recently, paclitaxel-eluting balloon angioplasty was shown to be superior to uncoated balloon angioplasty for the treatment of ISR after BMS and DES (18–20). Although the mechanism of ISR in SF sites has not been fully evaluated, an

OCT study showed that neointimal hyperplasia is increased at fracture sites after SES implantation (21). Therefore, paclitaxel-eluting balloon angioplasty might be an alternative treatment for SF lesions. Most importantly, however, clinicians should select DES with a lower tendency to fracture in lesions at high risk for SF. Taking the results of the present and previous studies into consideration, PtCr-EES might become the first-choice DES for such lesions.

STUDY LIMITATIONS. First, this study was a single-center study, and follow-up angiography was not performed in all patients. Therefore, selection bias may exist in the present study and may have biased the conclusion. Second, IVUS and OCT were not performed in all patients undergoing follow-up angiography. In addition, the detection of partial SF on angiogram was limited because of its spatial resolution, regardless of high visibility on plain fluoroscopy of PtCr-EES. Therefore, the present study may have underestimated the incidence of SF. Third, despite the fact that we selected modeling variables using the tight criteria of $p < 0.05$, instead of the usually adopted $p < 0.10$ or 0.20, the findings from multivariable modeling with 4 variables should be interpreted with caution because of the small number of patients with fracture ($n = 16$). Our sensitivity analysis of random-intercept logistic regression using other combinations among finally selected 4 variables showed that the estimated OR varied in some magnitude, but their direction and p values were stable throughout almost all the models (Online Table 2). We also fitted the model (without random effects) via Firth's penalized likelihood and an exact method, which provided essentially the same OR estimates and p values. Finally, the association between ISR and SF was marked in the present study. It might be due to ascertainment bias, that is, ISR lesions were more carefully scrutinized for evidence of SF.

CONCLUSIONS

SF after PtCr-EES implantation occurs in 1.7% of lesions and appears to be associated with clinically driven TLR. Lesions with ISR or hinge motion and the total stent length are predictors of SF.

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PERSPECTIVES

WHAT IS KNOWN? SF is still an unresolved, clinically relevant issue even in the newer-generation DES era. PtCr-EES is a newer-generation DES that uses the same drug and polymer as CoCr-EES but combines them with a novel metal alloy and stent design intended to improve fracture resistance. However, the incidence and clinical impact of SF after PtCr-EES implantation remain unclear.

WHAT IS NEW? A total of 700 patients with 898 lesions undergoing PtCr-EES implantation were analyzed. SF was observed in 16 of 898 lesions (1.7%). Lesions with ISR at baseline or hinge motion, and total stent length were predictors of SF. The cumulative incidence of clinically driven TLR within 9 months after the index procedure was numerically higher in the SF group than that in the non-SF group (18.7% vs. 2.3%), whereas definite ST did not occur in the SF group.

WHAT IS NEXT? PtCr-EES may reduce the incidence of SF to the utmost limit of a metallic DES.

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KEY WORDS drug-eluting stent fracture, platinum-chromium everolimus-eluting stent, target lesion revascularization

APPENDIX For a supplemental figure and tables, please see the online version of this paper.